States Patent Application Serial No. 07/738,040, filed July 30, 1991; a continuation-in-part of United States Patent Application Serial No. 07/750,579, filed August 28, 1991, which is a continuation-in part of United States Patent Application Serial No. 07/559,955, filed July 31, 1990, which is a continuation-in-part of United States Patent Application Serial No. 07/472,070, filed January 30, 1990, which is a continuation-in-part of United States Patent Application Serial No. 07/388,044, filed July 31, 1989. --;

Page 16, line 13, replace "Figure descriptions continued at page 144." with -- Fig. 21: Binding affinity of Fab fragment SP2 for recombinant human thyroid peroxidase (TPO). Brackets indicate the mean ± the range of duplicate densitometric values obtained for each TPO concentration in a representative experiment. Comparable results were obtained in two additional experiments.

Figures 27A to 27B: Fig.27A. Effect of increasing molar (M) concentrations of TPO, lactoperoxidase (LPO) or myeloperoxidase (MPO) on the binding of ^{125} I-TPO by SP1.2. Background binding in the absence of Fab fragments (~2%) was subtracted. Fig.27B. Competition inhibition by unlabeled TPO of radiolabeled TPO binding to the Fab fragments. In the absence of unlabeled TPO, binding values for the three Fab fragments were 13-15%. Background of ~2% was subtracted. Dissocation constants (Kd) were determined by Scatchard analysis (Scatchard, G., "The attractions of proteins for small molecules and ions," Ann. NY Acad. Sci. VOL 51:660-672 (1949)) and are:

SP2 =8.3×10^{-11}M ; SP4 = 2.2×10^{-10}M; SP5 = 3×10^{-11}M

Figure 28: Inhibition by increasing molar (M) concentrations of SP1.2 on the binding to ^{125} I-TPO by serum TPO autoantibodies. The mean values (± S.E.M.) obtained for sera from 11 patients are shown by solid circles. Background binding by serum from a TPO autoantibody negative donor was not subtracted and is shown by the open circles (mean ± S.E.M. of 3 experiments).

Figures 29A to 29C: Competition ELISA for binding to TPO between the SP1.2 Fab fragment and TPO autoantibodies of different IgG subclasses. Figs. 29A to 29C show data obtained with three different patients. TPO autoantibody levels are shown as the 0.D. readings measured at 492nm. Background O.D. values obtained for TPO autoantibody-negative serum were <0.05. SP1.2 (M); molar concentration of SP1.2.

Figures 30A to 30B: Effect of denaturation of TPO on SP Fab fragment binding. Binding of SP1.2, SP1.4 and SP1.5 Fig. 30A or mouse monoclonal antibody #40.28 Fig. 30A was measured to native or denatured TPO by ELISA. Binding is shown as the O.D. value at 492nm. Background O.D. values for TPO autoantibody negative serum and control murine ascites were <0.05.

Figure 33: Binding domains on TPO for the SP1.2, SP4.6, SP1.20 F(ab)s. ^{125}I-TPO was preincubated in the absence or presence of increasing concentrations of SP4.6, SP1.20 or SP1.2 [Free F(ab)]. The ability of these complexes to bind to immobilized SP1.2 was then determined. The results are expressed as % 1251-TPO bound after subtraction of background values (~ 2%) obtained using buffer alone.

Figures 36A to 36D: Domains on TPO recognized by F(ab)s. Increasing concentrations of one F(ab) were pre-incubated with radiolabelled TPO and then added to a second, immobilized F(ab) (Methods). The immobilized F(ab) was TRI.9 Fig. 36A, TR1.7 Fig 36C and SP1.5 Fig 36D. The ability of the free F(ab) to inhibit binding to itself is shown by the open circles. Confirmation of the binding potency of the free F(ab)s was determined concurrently in each experiment. A representative control Fig. 36B for the experiment in Fig. 36A. is shown.

Figure 37: Schematic representation of the binding domains on TPO for the expressed F(ab)s.

Figures 38A to 38C: Domains on TPO recognized by autoantibodies in 3 representative sera Figs. 38A ,38B and 38C from patients with autoimmune thyroid disease. F(ab)s WR1.7 and TR1.9, alone or in combination, were used to compete for serum autoantibody binding to radiolabeled TPO (Methods).--;

Delete pages 144 through 149 in their entirety;

Page 18, line 17, after "fragment thereof." insert -- For example, a substantially pure recombinant thyroid peroxidase, wherein a nine amino acid region comprising residues 713-721 of recombinant human thyroid peroxidase, have been deleted or replaced may be an analog of the recombinant thyroid peroxidase with the intact original amino acids in the 713 -721 region. --;

Delete Drawings Figure 22 and Figure 22 (cont.) in their entirety;

Delete Drawing Figure 23 in its entirety;

Delete Drawings Figure 24 and Figure 24 (cont.) in their entirety;

Delete Drawing Figure 25 in its entirety;

Delete Drawing Figure 26 in its entirety;

Delete Drawings Figure 31A, Figure 31A (cont.) Figure 31B and Figure 31C in their entirety;

Delete Drawings Figure 32A and 32B in their entirety;

Delete Drawings Figure 34 and Figure 34 (cont.) in their entirety;

Delete Drawings Figure 35 and Figure 35 (cont.) in their entirety.

IN THE CLAIMS

Please amend the following claims:

38. (Amended) A recombinant DNA sequence encoding a human thyroid peroxidase, [which] the human thyroid peroxidase is recognized by [a disease associated antibody] an antibody associated with thyroiditis.

48. (Amended) A recombinant DNA sequence encoding a human thyroid peroxidase which is secreted from a cell and is recognized by [a disease associated antibody] an antibody associated with thyroiditis.

Please add the following claims:

58. (New) The recombinant DNA sequence of claim 38 wherein the antibody is associated with Hashimoto's thyroiditis.

59. (New) The recombinant DNA sequence of claim 48 wherein the antibody is associated with Hashimoto's thyroiditis.